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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/553,570

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Kenneth Hinds

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EXAMINER

ROBINSON, HOPE A

ART UNIT

PAPER NUMBER

1652

MAIL DATE

DELIVERY MODE

07/16/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/553,570	Applicant(s) HINDS ET AL.	
	Examiner HOPE A. ROBINSON	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 March 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 and 17-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 and 17-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 October 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/1/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

1. Applicant's election with traverse of Group I is acknowledged.
2. The traversal is on the grounds that Group I encompass claims 12-13 and 17. For clarity, it is noted that some claims contained in Group I were inadvertently left off the restriction group. Thus pending claims 12-13 and 17-20 are also contained in Group I and are herein under examination.

Claim Disposition

3. Claims 14-16 and 21-31 have been canceled. Claims 1-13 and 17-20 are pending and are under examination.
4. The Amendments filed on October 6, 2005 and March 31, 2009 has been received and entered.

Specification

5. The specification is objected to because of the following informalities:

The specification is objected to because trademarks are disclosed throughout the instant specification and not all of them are capitalized or accompanied by the generic terminology. The use of the trademarks such as TWEEN-20TM, for example, have been noted in this application (see page 22). It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following is suggested: "A method for preparing protein-polymer conjugates".

The specification is objected to because the first page does not mention that the instant application is a 371 of PCT/US04/10995.

Correction is required.

Drawing

6. The drawings filed on October 6, 2005 are accepted by the examiner.

Information Disclosure Statement

7. The Information Disclosure Statement filed on May 1, 2006 has been received and entered. The references cited on the PTO-1449 Form have been considered by the examiner and a copy is attached to the instant Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-13 and 17-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to a method for preparing a protein- polymer conjugate or insulin-PEG conjugate (see claims 1 and 18) and the claims refer to “conditions that promote the formation of a conjugate”, however, none is presented in

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the instant specification. For example, at paragraph [0039] in the specification, it is disclosed that, "in accordance with the present invention, the insulin protein and hydrophilic polymer are contacted (i.e., reacted or conjugated) in the presence of at least one organic solvent and at least one metal chelator, under conditions that promote the formation of a conjugate of the protein and polymer. In a particular embodiment, the insulin protein is PEGylated at the PheB1 amino terminus using minimum PEG reagent and mild conditions. The amino group of PheB1 is normally the least reactive of the 3 available amino functions on insulin (Caliceti et al., 1999, supra). In the present invention, conditions have been found that render the PheB1 amino group the most reactive to PEG reagents. These reaction conditions thus produce single PEGylation at the PheB1 as the predominant reaction product". As the claims are directed to a method of producing a specific conjugate, adequate written description should be provided as to the conditions of the invention that promote such an occurrence.

In addition, the claimed invention is directed to a genus of "amino reactive derivatives thereof" (see for example claim 3) that are not adequately described. The specification fails to provide any additional representative species of the claimed genus to show that applicant was in possession of the claimed genus. A representative number of species means that the species which are adequately described are representative of the entire genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, disclosure of drawings, or by disclosure of relevant identifying characteristics, for example, structure or other physical and/or

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chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Moreover, *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991), states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993).

Therefore, for all these reasons the specification lacks adequate written description, and one of skill in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 1-13 and 17-20 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claim 1 is indefinite for the recitation of “ under conditions that promote the formation of a conjugate” as it is unclear what “conditions are being referred to. At paragraph [0039] in the specification, it is disclosed that, "in accordance with the present invention, the insulin protein and hydrophilic polymer are contacted (i.e., reacted or conjugated) in the presence of at least one organic solvent and at least one metal chelator, under conditions that promote the formation of a conjugate of the protein and polymer. In a particular embodiment, the insulin protein is PEGylated at the PheB1 amino terminus using minimum PEG reagent and mild conditions. The amino group of PheB1 is normally the least reactive of the 3 available amino functions on insulin (Caliceti et al., 1999, supra). In the present invention, conditions have been found that render the PheB1 amino group the most reactive to PEG reagents. These reaction conditions thus produce single PEGylation at the PheB1 as the predominant reaction product”. Note however that the "conditions" are not really presented in the discussion, thus the metes and bounds of the claim is unclear.

Claim 3 is indefinite because the claim represents an improper Markush claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Lewis et al. (US Patent No. 6,706,289, October 31, 2001).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention “by another,” or by an appropriate showing under 37 CFR 1.131.

Lewis et al. teach a preparation of polyethylene glycol conjugated to human insulin (see paragraph 43). The polymer taught by Lewis et al. is hydrophilic (see paragraph 1). Paragraph 30 of the patent discloses that the polymer is dissolved in an organic solvent. At paragraph 12 of the patent the use of DMSO is disclosed in a concentration as disclosed by the instant application. Lewis et al. teaches a pH within the 5-7 range recited in the claims (see paragraphs 9 and 27). In addition, a

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temperature within the recited range is disclosed at paragraph 27 of the patent.

Therefore, the limitations of the claims are met by the reference.

Conclusion

11. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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/Hope A. Robinson/

Primary Examiner, Art Unit 1652